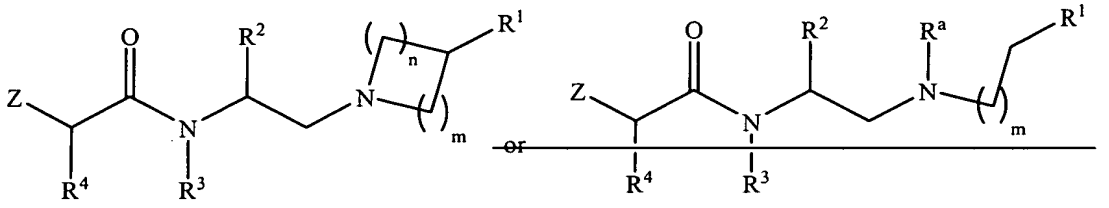
This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. ***(currently amended)*** A compound of formula Ia ~~**or Ib**~~:



Ia or Ib

;

wherein:

R^1 is H or OH;

~~**R^a is alkyl;**~~

R^2 is alkyl, aryl, or aralkyl;

R^3 is alkyl, or R^2 and R^3 taken together with the atoms through which they are connected form a 4- to 8-membered heterocyclic ring;

R^4 is H, alkyl, cycloalkyl, alkylcycloalkyl, aryl, aralkyl, heteroaryl, or heteroarylalkyl;

Z is $-(CH_2)_o-NR^5R^6$ or $-(CH_2)_o-C(=O)NR^7R^8$;

R^5 is H, alkyl, or aryl;

R^6 is aryl, alkaryl, $-CO(NH)_pR^9$, or $-SO_2R^9$, provided that at least one of R^5 and R^6 is other than aryl;

R^7 is H or alkyl;

R^8 is alkyl, aryl, aralkyl, alkaryl, heteroaryl, heteroarylalkyl, cycloalkyl or cycloalkylalkyl;

R^9 is alkyl, cycloalkyl, alkylcycloalkyl, aryl, aralkyl, heteroaryl, or heteroarylalkyl;

m is the integer 1, 2, or 3;

n is the integer 1, 2, or 3;

o is the integer 0, 1, 2, or 3;

p is the integer 0 or 1; and

the quantity (m + n) is an integer in the range of 2 to 5;

or a stereoisomer, prodrug, pharmaceutically acceptable salt, hydrate, solvate, acid salt hydrate, N-oxide or isomorphic crystalline form thereof.

2. ***(original)*** A compound according to claim 1, wherein the quantity (m + n) is 3.

3. ***(original)*** A compound according to claim 1, wherein o is the integer 0 or 1.

4. ***(original)*** A compound according to claim 1, wherein R^1 is –OH.

5. ***(original)*** A compound according to claim 1, wherein R^2 is aryl.

6. ***(original)*** A compound according to claim 5, wherein the R^2 is phenyl.

7. ***(original)*** A compound according to claim 1, wherein R^2 is alkyl.

8. ***(original)*** A compound according to claim 7, wherein R^2 is prop-2-yl.

9. ***(original)*** A compound according to claim 1, wherein R^3 is methyl.

10. ***(original)*** A compound according to claim 1,

wherein R^2 and R^3 taken together with the atoms through which they are connected form a 4- to 8-membered heterocyclic ring.

11. ***(original)*** A compound according to claim 10,
wherein R^2 and R^3 taken together with the atoms through which they are connected form a 5- to 6-membered heterocyclic ring.

12. ***(original)*** A compound according to claim 1,
wherein R^4 is H.

13. ***(original)*** A compound according to claim 1,
wherein Z is $-NR^5R^6$ or $-(CH_2)_o-C(=O)NR^7R^8$.

14. ***(original)*** A compound according to claim 13,
wherein R^5 is alkyl or aryl.

15. ***(original)*** A compound according to claim 14,
wherein the R^5 is methyl or phenyl.

16. ***(original)*** A compound according to claim 1,
wherein R^5 is H.

17. ***(original)*** A compound according to claim 1,
wherein R^6 is aryl.

18. ***(original)*** A compound according to claim 17,
wherein R^6 is phenyl.

19. ***(original)*** A compound according to claim 18,
wherein R^6 is phenyl substituted with -CN, $-NO_2$, $-NHS(=O)_2$(alkyl), halo, or $-CF_3$.

20. ***(original)*** A compound according to claim 18, wherein R^6 is phenyl substituted with chloro.

21. ***(original)*** A compound according to claim 1, wherein R^6 is alkaryl.

22. ***(original)*** A compound according to claim 1, wherein R^7 is H.

23. ***(original)*** A compound according to claim 1, wherein R^9 is alkyl.

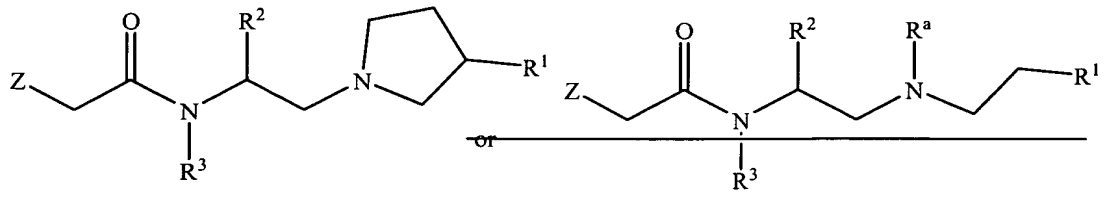
24. ***(original)*** A compound according to claim 23, wherein p is 0.

25. ***(original)*** A compound according to claim 1, wherein R^9 is aryl.

26. ***(original)*** A compound according to claim 25, wherein p is 1.

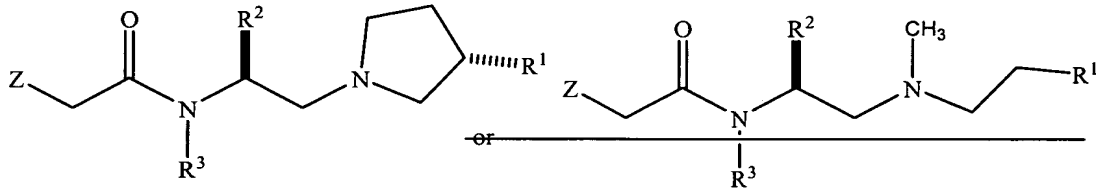
27. ***(original)*** A compound according to claim 26, wherein R^9 is phenyl.

28. ***(currently amended)*** A compound according to claim 1, of formula IIa ~~**or IIb**~~:



IIa or IIb

29. ***(currently amended)*** A compound according to claim 28, of formula IIc ~~or IId~~:



IIc or IId

30. ***(original)*** A compound according to claim 29,

wherein:

R^2 is aryl or alkyl;

R^3 is alkyl;

Z is $-NR^5R^6$ or $-(CH_2)_o-C(=O)NR^7R^8$;

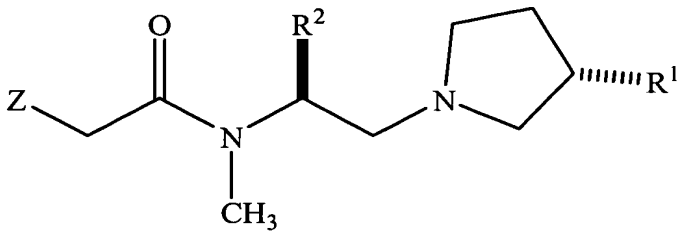
R^7 is H;

R^8 is aryl, aralkyl, heteroaryl, or alkaryl; and

o is the integer 0 or 1.

31. ***(original)*** A compound according to claim 30, wherein R^6 is aryl, alkaryl, or $-CO(NH)_pR^9$.

32. ***(original)*** A compound according to claim 30 of formula III:



III

33. ***(original)*** A compound according to claim 32,
wherein:
R^1 is OH;
R^2 is phenyl or prop-2-yl;
R^5 is H, methyl, or phenyl; and
R^9 is alkyl.

34. ***(original)*** A compound according to claim 33,
wherein:
R^2 is phenyl;
R^5 is H;
R^6 is phenyl or *meta*-methylphenyl;
R^7 is H; and
R^8 is phenyl or heteroaryl.

35. ***(original)*** A compound according to claim 34,
wherein Z is NH(phenyl).

36. ***(original)*** A compound according to claim 35,
wherein the phenyl in Z is substituted with $-NHS(=O)_2$-alkyl.

37. ***(original)*** A compound according to claim 36,
wherein the alkyl in $-NHS(=O)_2$-alkyl is methyl.

38. ***(original)*** A compound according to claim 36,
wherein the alkyl in -NHS(=O)$_2$-alkyl is n-propyl.

39. ***(original)*** A compound according to claim 35,
wherein the phenyl in Z is unsubstituted.

40. ***(original)*** A compound according to claim 34,
wherein Z is -CH_2C(=O)NH(unsubstituted phenyl).

41. ***(original)*** A compound according to claim 34,
wherein Z is -C(=O)NH(unsubstituted phenyl).

42. ***(cancelled)***

43. ***(currently amended)*** A compound according to claim 1, wherein said compound is:
N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-2-phenylamino-acetamide;
N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-2-(methyl-phenyl-amino)-acetamide;
2-(acetyl-phenyl-amino)-N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl]-(S)-1-phenyl-ethyl}-N-methyl-acetamide;
2-(4-cyano-phenylamino)-N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-acetamide;
2-(3-cyano-phenylamino)-N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-acetamide;
2-(2-cyano-phenylamino)-N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-acetamide;
2-(4-aminomethyl-phenylamino)-N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-acetamide;
2-[(4-cyano-phenyl)-methyl-amino]-N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-acetamide;

N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-2-[4-(methanesulfonylamino-methyl)-phenylamino]-N-methyl-acetamide;

N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-2-[3-(methanesulfonylamino-methyl)-phenylamino]-N-methyl-acetamide;

N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-2-[2-(methanesulfonylamino-methyl)-phenylamino]-N-methyl-acetamide;

2-(3,4-dichloro-phenylamino)-N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-acetamide;

2-(4-trifluoromethyl-phenylamino)-N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-acetamide;

2-[(2,4-dichloro-phenyl)-methanesulfonyl-amino]-N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-acetamide;

2-(4-nitro-phenylamino)-N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-acetamide;

N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-2-(4-methanesulfonylamino-phenylamino)-N-methyl-acetamide;

N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-2-(4-propanesulfonylamino-phenylamino)-N-methyl-acetamide;

N-{(S)-1-[(S)-3-hydroxy-pyrrolidin-1-ylmethyl]-2-methyl-propyl}-N-methyl-2-[4-(propane-1-sulfonylamino)-phenylamino]-acetamide;

propane-1-sulfonic acid (4-{2-[2-(S)-{(S)-3-hydroxy-pyrrolidin-1-ylmethyl}-piperidin-1-yl]-2-oxo-ethylamino}-phenyl)-amide;

N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-N'-phenyl-malonamide;

~~**N-{2-[(2-hydroxy-ethyl)-methyl-amino]-(S)-1-phenyl-ethyl}-N-methyl-N'-phenyl-malonamide;**~~

N-[4-(methanesulfonylamino-methyl)-phenyl]-N'-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N'-methyl-malonamide;

N-[4-(ethanesulfonylamino-methyl)-phenyl]-N'-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N'-methyl-malonamide;

N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N'-(4-methanesulfonylamino-phenyl)-N-methyl-malonamide;

N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-N'-[2-(pyrrolidine-1-sulfonyl)-phenyl]-malonamide;

N-benzyl-N'-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N'-methyl-malonamide;

N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-N'-thiazol-2-yl-malonamide;

N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-N'-pyridin-3-yl-malonamide;

N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-N'-phenyl- succinimide;

N-[(S)-1-{(S)-3-hydroxy-pyrrolidin-1-ylmethyl}-2-methyl-propyl]-N-methyl-N'-phenyl-succinamide;

4-{(S)-2-[(S)-3-hydroxy-pyrrolidin-1-ylmethyl]-piperidin-1-yl}-4-oxo-N-phenyl-butyramide;

N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-N'-thiazol-2-yl-succinamide;

N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-N'-pyridin-3-yl-succinamide;

N-{2-[(S)-3-hydroxy-pyrrolidin-1-yl]-(S)-1-phenyl-ethyl}-N-methyl-2-(3-phenyl-ureido)-acetamide;

N-[(S)-1-{(S)-3-hydroxy-pyrrolidin-1-ylmethyl}-2-methyl-propyl]-N-methyl-2-(3-phenyl-ureido)-acetamide;

4-{(S)-2-[(S)-3-hydroxy-pyrrolidin-1-ylmethyl]-piperidin-1-yl}-4-oxo-N-phenyl-butyramide; or

a stereoisomer, a prodrug, a pharmaceutically acceptable salt, a hydrate, a solvate, an acid salt hydrate, an N-oxide or an isomorphic crystalline form thereof.

44. ***(original)*** A pharmaceutical composition, comprising:

at least one pharmaceutically acceptable carrier; and

at least one compound according to claim 1.

45. ***(original)*** A pharmaceutical composition according to claim 44, further comprising at least one opioid.

46. ***(original)*** A pharmaceutical composition according to claim 45,

wherein said opioid is selected from the group consisting of alfentanil, buprenorphine, butorphanol, codeine, dezocine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanol, meperidine (pethidine), methadone, morphine, nalbuphine, oxycodone, oxymorphone, pentazocine, propiram, propoxyphene, sufentanil, tramadol, and mixtures thereof.

47. ***(original)*** A pharmaceutical composition according to claim 44, further comprising at least one compound selected from the group consisting of antibiotics, antivirals, antifungals, anti-inflammatories, anesthetics, and mixtures thereof.

48. ***(withdrawn)*** A method of binding opioid receptors in a patient in need thereof, comprising the step of:

administering to said patient an effective amount of at least one compound according to claim 1.

49. ***(withdrawn)*** A method according to claim 48,

wherein said compound does not substantially cross the blood-brain barrier.

50. ***(withdrawn)*** A method according to claim 48,

wherein said patient is in need of an analgesic.

51. ***(withdrawn)*** A method according to claim 48,

wherein said compound binds κ opioid receptors.

52. ***(withdrawn)*** A method according to claim 51,

wherein said κ opioid receptors are located in the central nervous system.

53. ***(withdrawn)*** A method according to claim 51,

wherein said κ opioid receptors are located peripherally to the central nervous system.

54. ***(withdrawn)*** A method according to claim 51,

wherein said binding agonizes the activity of said opioid receptors.

55. ***(withdrawn)*** A method for preventing or treating gastrointestinal dysfunction, comprising the step of:

administering to a patient in need of such treatment, an effective amount of at least one compound according to claim 1.

56. ***(withdrawn)*** A method for preventing or treating ileus, comprising the step of:

administering to a patient in need of such treatment, an effective amount of at least one compound according to claim 1.

57. ***(withdrawn)*** A method of preventing or treating pain, comprising the step of:

administering to a patient in need of such treatment, an effective amount of at least one compound according to claim 1.

58. ***(withdrawn)*** A method according to claim 57, further comprising the step of:

administering an effective amount of at least one opioid.

59. ***(withdrawn)*** A method according to claim 58,

wherein said opioid is selected from the group consisting of alfentanil, buprenorphine, butorphanol, codeine, dezocine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanol, meperidine (pethidine), methadone, morphine, nalbuphine, oxycodone, oxymorphone, pentazocine, propiram, propoxyphene, sufentanil, tramadol and mixtures thereof.

60. ***(withdrawn)*** A method for preventing or treating pruritic dermatoses and conditions characterized by pruritic dermatosis as a symptom, comprising the step of:

administering to a patient in need of such treatment, an effective amount of at least one compound according to claim 1.

61. ***(withdrawn)*** A method according to claim 60,

wherein said pruritic dermatosis is selected from the group consisting of allergic dermatitis, atopy, contact dermatitis, psoriasis, eczema, opioid-induced pruritus, and insect bites.

62. ***(withdrawn)*** A method for preventing or treating cerebral edema, comprising the step of:

administering to a patient in need of such treatment, an effective amount of at least one compound according to claim 1.

63. ***(withdrawn)*** A method for preventing or treating oxygen supply deficiency of the central nervous system, comprising the step of:

administering to a patient in need of such treatment, an effective amount of at least one compound according to claim 1.

64. ***(withdrawn)*** A method for inducing diuresis, comprising the step of:

administering to a patient in need of such treatment, an effective amount of at least one compound according to claim 1.

65. ***(withdrawn)*** A method for preventing or treating tussis, comprising the step of:

administering to a patient in need of such treatment, an effective amount of at least one compound according to claim 1.